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Vertebral Fractures Assessment in Children: Evaluation of DXA imaging versus Conventional Spine Radiography

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ABSTRACT

Vertebral fracture assessment (VFA) by DXA is an accepted tool in adults. However, its use in children has not been assessed. The aim of this study was to evaluate DXA VFA and morphometric analysis (MXA) using a GE Lunar iDXA bone densitometer against spinal radiographic assessment (RA) for the identification of vertebral fractures in children.

Spine RA and VFA (T3-L5) were acquired on the same day in 80 children. Forty children considered high risk for fracture by their metabolic bone specialist were referred for spinal RA. Another 40 children were recruited as part of a prospective fracture study and were considered low risk for vertebral fracture. Agreement between RA and VFA was assessed by an expert paediatric radiologist and two paediatricians with expertise in bone pathology. Agreement between RA and MXA was assessed by an expert paediatric radiologist, two clinical scientists and an experienced paediatric radiographer. Vertebrae were ranked as normal, mild, moderate or severe if they had <10%, 11-25%, 26-50% and >50% deformity, respectively. Levels of agreement were calculated using the Cohen kappa score.

Evaluating the data from all readable vertebrae, 121 mild, 44 moderate and 16 severe vertebral fractures were identified; with 26, 8, and 5 subjects having at least one mild, moderate or severe fracture, respectively. Depending on rater, 92.8-94.8% of the vertebrae were evaluable by RA. In contrast, 98.4% were evaluable by VFA and only 83.6% were evaluable by MXA. Moderate agreement was found between raters for RA [kappa 0.526-0.592], and VFA [kappa 0.601-0.658] and between RA and VFA [kappa 0.630-0.687]. In contrast, only slight agreement was noted between raters for MXA [kappa 0.361-0.406] and between VFA and MXA [kappa 0.137-0.325]. Agreement substantially improved if the deformities were dichotomised as normal or mild versus moderate or severe [Kappa 0.826-0.834]. For the detection of moderate and/or severe fractures the sensitivities & specificities were 81.3% & 99.3%, and 62.5% & 99.2% for VFA and MXA, respectively.

This study demonstrates that VFA is as good as RA for detecting moderate and severe vertebral fractures. Given the significant radiation dose saving of VFA compared with RA, VFA is recommended as a diagnostic tool for the assessment of moderate or severe vertebral fracture in children.

KEY WORDS: Vertebral Fracture Assessment; Fracture; Paediatric; Bone Density; DXA; X-ray.

CONFLICT OF INTEREST: None

INTRODUCTION

Vertebral fracture assessment (VFA) by dual-energy X-ray absorptiometry (DXA) is a proven clinical tool to diagnose vertebral deformities and fractures in an adult population [1]. Previous work suggested that with older generations of DXA scanners VFA may not be suitable in children[2]. However, with the advance of newer, high-resolution, bone densitometers it may now be possible to extend this diagnostic procedure for use in paediatrics.

The identification of vertebral fractures in children has become increasingly important as a consequence of the observation that fractures are not necessarily associated with reduced bone mineral density (BMD) as measured by DXA[3]. This has led to a change in the definition of osteoporosis in children by the International Society for Clinical Densitometry (ISCD), which states that the presence of one or more vertebral fractures is consistent with osteoporosis regardless of BMD[4].

Using serial plain spinal radiographic assessment (RA), the Canadian prospective STOPP study recently published prevalence and incident fracture rates in children on glucocorticoids for different conditions. Seven percent of children with rheumatic conditions had vertebral fractures identified even before, or within 30 days of, initiation of corticosteroid therapy [5]. From the same study, 16% of children newly diagnosed with acute lymphoblastic leukaemia (ALL) had vertebral compression fractures predominantly located in the thoracic spine [6]. Therefore, early detection of vertebral fracture is essential for clinical management, in particular since such fractures may often be asymptomatic [7]. To date, VFA in children has relied largely on spinal RA which comes with high radiation exposure (150-300µSv)[8]. Since DXA VFA can be performed at substantially lower radiation doses (10-40µSv)[9], this technology lends itself to use in paediatrics.

Whilst the first paediatric study [2] reported poor image resolution and lower diagnostic accuracy of VFA from DXA-derived images compared to RAs, a later study [10] concluded that VFA reliably identified moderate and severe fractures in children with osteogenesis imperfecta. Similarly, using a different model of DXA scanner, a clinical audit of 20 children demonstrated excellent agreement between RA and VFA-MXA with good inter-operator agreement. However, they concluded that whilst VFA was a useful fracture screening tool, plain radiographs are needed to confirm the diagnosis [11].

Over the last decade, substantial improvements in image resolution have been afforded to bone densitometers, which now have the potential to expand the diagnostic utility of DXA. Therefore, the aim of this study was to evaluate vertebral fracture assessment (VFA) and morphometric analysis (MXA) in a cohort of children with a chronic disease, using the latest DXA imaging technology against spinal RA for the identification of vertebral fractures in children.

Materials and Methods

Subjects

The study population consisted of 80 children, mean age 12 years (5.1 to 18.8 years), 40 of whom were identified from routine metabolic bone clinics at Birmingham Children's Hospital. Another 40 children were recruited from the 'SNAP' study, a separate prospective fracture study in children and adolescents with chronic inflammatory and/or disabling conditions (National Institute of Health Research Clinical Development Fellowship (HCS/P10/009)). The 40 children recruited from clinic had been identified as being at risk of vertebral fracture and consequently had a clinical referral for both a conventional lateral lumbar-thoracic radiograph as well as DXA, and had the DXA VFA performed as an

additional investigation. The 40 ‘SNAP’ patients had conventional lateral lumbar-thoracic radiographs and DXA VFA as part of the prospective study research protocol. All subjects had lateral DXA images of the spine from T3 to L5 acquired using a Lunar GE iDXA bone densitometer (GE Lunar Corp. Madison, WI, USA) and conventional radiographs acquired using a Wolverson Acoma (Wolverson X-ray Ltd, Willenhall, UK) on the same day. VFA images were acquired using standard machine protocol; the patient was positioned in the decubitus position with their arms above their head and their spine completely flat against the supplied VFA positioner. Foam padding was used, where necessary, to reduce any sagging around the waist, and between the knees and ankles, to reduce spinal rotation. RA images were acquired according to European Guidelines [12]. The patient was also placed in the decubitus position with their arms above their head. Depending on patient size, either thoracolumbar or separate thoracic and lumbar exposures were taken. Beam coning techniques were used to minimize radiation exposure.

All subjects had lumbar spine and total body bone density measurements performed using a GE Lunar iDXA™ bone densitometer (software version 13.6) as part of their standard fracture risk assessment. Prior to scanning, the child’s height (to the nearest 0.1 cm) was measured using a wall-mounted stadiometer and weight (to the nearest 0.1 kg) was measured using hospital balance scales. All measurements were made with the children in light indoor clothes or a hospital gown, without shoes. South Birmingham Research Ethics Committee approved this study and either the child’s parent or guardian or the patients themselves, if over 16 years, signed informed consent (REC reference number: 10/H120718). All research was carried out in accordance with the Declaration of Helsinki.

Image Analysis

RA and VFA images (**Figure 1**) were independently evaluated by an expert paediatric radiologist (R1) and two paediatricians with expertise in metabolic bone disease (R2, R3). In

order to reduce observer bias, RA & VFA images were analysed on different days, in a random order without access to the subject's clinical information and BMD results, and also blinded to any previous analysis. The 'gold standard' was considered to be the fracture confirmation and classification from the conventional radiographs made by the expert paediatric radiologist (R1), as this is the most commonly used conventional technique for vertebral fracture detection. Vertebral fractures were classified using a modified Genant semi-quantitative approach [9]; a simplified classification was utilised in order to make the assessment quick and easy to use. Mild fractures were classified as a height reduction of more than 10% but less than 25% in either the anterior, posterior or mid-vertebral height. Moderate fractures were identified when there was more than 25% but less than 50% height reduction, while severe fractures had a height reduction greater than 50% (**Figure 2**). Data analysis was split into two groups; those with any identifiable fractures (Any-fracture) i.e. those with greater than 10% vertebral height reduction (Mild/Moderate/Severe) [13] and those with a clinically significant osteoporotic fracture (Clinical-fracture) i.e. greater than 25% vertebral height reduction (Moderate/Severe) [14].

Morphometric Analysis

An experienced clinical scientist (R4), a senior radiographer (R5) and a clinical scientist unfamiliar with VFA (R6) performed semi-quantitative DXA VFA in addition to morphometric analysis of the DXA acquired images. The scientist (R4) and the radiologist (R1) provided technique training prior to commencing the study. Semi-quantitative VFA was performed as previously described [9]. The results were compared to the 6-point morphometric analysis (MXA) where the operator places 6 points on each vertebra corresponding, respectively, to the four corners of the vertebral body and the mid point of the vertebral end plate. From the point placement the software estimates, anterior (Ha), mid (Hm)

and posterior (Hp) vertebral heights for each vertebra from T4 to L4. The heights were then used to calculate the following ratios Ha/Hp, Hm/Hp, Hp/Hp^{+1} or Hp/Hp^{-1}, where Hp^{+1} and Hp^{-1} signify the vertebra directly above or below Hp. Each vertebra was classified as normal or as having a mild, moderate or severe deformity, if the ratio was greater than 0.90, between 0.91 and 0.75, between 0.76 and 0.50 and less than 0.51, respectively.

Radiation Dosimetry

The radiation doses for lateral spinal radiographs (thoracic and lumbar spine or whole spine) and iDXA were calculated using the examination exposure factors and dose area product (DAP). DAP was recorded for the radiograph examinations and calculated for iDXA from the patient entrance surface dose (ESD) and scan area. These factors were used to provide age specific estimates of effective dose (E) using dose calculation software, PCXMC 2.0. Using the calculated E the average lifetime additional risk of cancer induction (age and sex dependant) due to these exposure was calculated using factors provided by the Health Protection Agency (HPA-CRCE-028) [15].

Statistical Analysis

Levels of agreement were calculated using the Cohen kappa statistic. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using the error matrix from a binary prediction model with radiographic analysis by an expert skeletal paediatric radiologist as the 'gold standard'. All statistical analyses were performed using SPSS version 22.0 (SPSS Corp., Armonk, NY) or Microsoft® Excel 2010. Data are presented as mean (SD), unless otherwise stated.

Results

Eighty children with a chronic inflammatory and/or disabling condition who were considered at risk of low trauma fracture were recruited (**Table 1**). Children had been diagnosed with inflammatory bowel disease (IBD, n=21), osteogenesis imperfecta (OI, n=15), Duchenne muscular dystrophy (DMD, n=14), acute lymphoblastic leukemia (ALL, n=8), cystic fibrosis (CF, n=6), rheumatological disorders (RD, n=5), coeliac disease (CD, n=5) and other conditions (bronchiectasis, idiopathic juvenile osteoporosis, galactosaemia, homocystinuria, nemaline myopathy, n=6). Seventeen children (21%) were either currently receiving or had previously received bisphosphonate treatment (7 Pamidronate, 7 Zoledronate & 3 Risedronate). Forty-nine of the 80 children (61%) had taken or were currently taking corticosteroids and 36 of the total population (45%) complained of back pain.

A total of 3,600 individual vertebral images (T3-L5, for three raters) were assessed for each of the imaging techniques; 6.7%, 1.6% and 16.4% were either not visible or not evaluable for RA, VFA and MXA, respectively. The majority of the non-evaluable vertebrae were in the thoracic region (**Figure 3**). In total, 121 mild, 44 moderate and 16 severe vertebral fractures were identified using the 'gold-standard' technique, RA by the experienced paediatric radiologist. The severity and location of these fractures are shown in **Figure 4**. The most severe fractures were usually present in the mid-thoracic region whereas the mild and moderate fractures were more uniformly distributed throughout the thoracic and lumbar spine. The number and severity of vertebral fractures was similar between RA and VFA. However, using MXA a greater number of mild fractures was identified compared to VFA and RA (**Table 2**). A similar pattern was seen when the vertebral fractures were evaluated per subject (**Table 3**).

The ability to identify vertebral fractures using each of the techniques was evaluated by three different raters and the degree of agreement was calculated using the Cohen kappa score (**Table 4**). There was very good agreement between techniques when identifying moderate or

severe fractures. In contrast, when identifying 'any-fracture', there was significantly poorer agreement, with the poorest agreement noted for MXA. No significant differences were seen between raters for all techniques evaluated (**Table 4**).

Table 5 highlights the agreement between RA (the 'gold standard'), and VFA by the expert paediatric radiologist and MXA by the experienced clinical scientist. A similar pattern of greater agreement for 'clinical –fracture' was observed in comparison to 'any-fracture'. VFA had the greatest sensitivity and specificity in the identification of 'clinical fracture' compared to MXA. The greatest number of false positive fracture identifications was seen for MXA for 'any-fracture' (**Table 5**).

The radiation dose calculations produced the following results; the mean DAP was 18.3μGym^2 (SD 4.7) for iDXA and 69μGym^2 (SD 63.6) for the radiographs. The average E was 42μSv for iDXA (female/male 5-9 years E=49μSv/E=49μSv, 10-19 years E=40μSv/E=39μSv) and 97μSv for the radiographs (female/male 5-9 years E=56μSv/E=70μSv, 10-19 years E=109μSv/E=124μSv). Using age- and sex-dependent risk factors the average additional lifetime risk of cancer induction for 5-9 years is 0.0007% and 0.0005% for iDXA, and 0.0008% and 0.0007% for the radiographs, for females and males respectively. For 10-19 years, the respective average additional lifetime risk of cancer induction is 0.0004% and 0.0003% for the iDXA, and 0.0012% and 0.0010% for the radiographs. For either imaging technique, the additional lifetime cancer risk is less than 1 in 80,000, which is regarded as very low risk (HPA-CRCE-028) [15].

Discussion

This study demonstrates that VFA is as good as conventional radiographs in identifying moderate and severe vertebral fractures, specifically in the thoracic region where the greatest number of fractures was identified. The inter-rater and inter-technique agreement was not

significantly different for RA and VFA, but was significantly poorer for MXA when identifying vertebral fractures of any severity. Importantly, VFA was not inferior to RA when identifying vertebral fractures and both were less specific when trying to discriminate mild fractures from normal vertebrae. The lack of inferiority of VFA compared with RA when assessing for vertebral fracture combined with a reduction in ionising radiation exposure provides evidence that VFA is a useful tool to aid the diagnosis of osteoporosis in children. The outcome of this study agrees with work published by others using alternative bone densitometers [10, 11] but contradicts earlier work [2].

Combining the outcome of the results from our study, with those from Diacinti et al. and Kyriakou et al, we have demonstrated that VFA, using the three different densitometers, is comparable to RA for identifying clinically significant osteoporotic fractures. All three densitometers showed good sensitivity, specificity, PPV and NPV with low rates of false negative and positive fracture identification. Compared to the previous studies we have shown better visualization of the thoracic spine by VFA (98.5%) than by RA (92.8%) [10]. Diacinti et al. reported that only 90.9% of the vertebrae were visible by VFA compared to 97.9% by RA. These differences in visualization of the vertebrae are likely related to differences in image acquisition and resolution of modern versus older generation scanners. Newer scanners using dual-energy x-rays in combination with improved detector resolution have improved visualization of the thoracic spine.

In our study we used RA as the gold standard for identification of vertebral fractures. However, in a recent publication from the STOPP consortium, which only used RA, there was only moderate agreement within and between three radiologists [16]. Similarly, we found only moderate agreement between raters using RA to identify any vertebral fracture. However, using both RA and VFA there was very good agreement between operators when

identifying moderate and severe fractures. In children with chronic disease, the commonest consequence of bony structural failure is vertebral fracture but there are no uniformly agreed criteria for their diagnosis [17]. This is particularly pertinent when trying to identify a mild prevalent vertebral fracture, as it is important to distinguish a true fracture from merely natural variation. Part of the problem is the lack of paediatric normative data and the lack of a true gold standard. Without a true gold standard one will always compare perceived best technique or current practice to newer approaches. A potentially more accurate standard would be MRI imaging of the spine reformatted in the mid-sagittal plane. This would allow evaluation of vertebral shape and height loss and also provide information on marrow signal change. However, due to the limited availability of MRI scanners, cost and poor patient tolerance, this technique is not clinically viable in most hospital settings.

The lack of robust reference data has resulted in a variety of different definitions for type and severity of vertebral fracture. The most commonly used thresholds in adults are those by Genant et al [9]. However, since then there have been several other classifications proposed [13, 18, 19] and assessment techniques developed, such as the algorithm based qualitative (ABQ) technique [14, 20, 21]. Gaca et al. reported that absolute height of a vertebra changed over time, but that the ratios of anterior to posterior heights remained constant at approximately 1[13]. As such, a height reduction of more than 10% was less likely to be considered normal variation and more likely to represent a fracture. Adiotomre et al. proposed a simplified ABQ technique to classify vertebrae as normal, fractured with less than 25% height loss, fractured with 25% or more height loss or non-osteoporotic deformity [14]. The threshold of 25% resulted from a UK based survey of paediatric bone specialists; 93% indicated that they were most likely to initiate treatment in patients with vertebral fractures with a height loss or 25% or more plus pain [14]. The thresholds used in this paper were based on a combination of Gaca [13] Adiotomre [14] and Genant [9]. Whilst there was

excellent agreement for vertebra with more than 25% height loss (clinical fracture), there was less agreement for vertebra with 10-25% height loss (mild fracture). The differences in fracture definition may account for the different agreement levels between all techniques. However, even using the higher threshold of a 20% cut off for mild fractures, Diacinti et al. found poor agreement between RA and VFA and VF and MXA[10].

Our MXA results are similar to those published in children [10, 11] and adults [22]. MXA uses the ratio of measured heights to ascertain whether a vertebra is fractured. Since operator subjectivity is removed from the assessment, one would expect the technique to be more robust than qualitative techniques. However, in practice, the placement of the points still heavily relies on the operator being able to clearly visualize the end plates. In the thoracic region where there is a great deal of image noise from overlying bony and soft tissue structures, the exact location of the endplate can be problematic. Compounding the imaging issues, is the use of ratios in the classification system. Subsequently, small differences in the absolute measures of vertebral height will have marked differences on calculated ratios. An absolute height difference of less than 1 mm may change the ratio from 0.89 to 0.91 and thus change a vertebra from being classified as normal into one with a mild fracture. In examples like this, other features such as end plate changes may influence the more experienced reader as to the existence of a fracture [14]. Currently, research into automated shape analysis using sophisticated computing is being developed for fracture identification in adults [23, 24]. Similar technology may prove useful in children where more information on normal variation and mild fractures is needed. Presently, the high false positive rate of MXA renders the technique unsuitable as a lone tool for the diagnosis of mild vertebral fractures in children.

The effective dose calculations demonstrated, as expected, that the radiation dose received from DXA VFA was on average half of that received from conventional radiographs.

Although the dose saving is less than predicted from previous work [8, 9] it still represents a significant dose saving. International principles state that diagnostic evaluations should always subject the patient to the lowest levels of ionising radiation as is reasonably practicable (ALARP) [25]. Hence, since VFA was shown not to be inferior to RA it follows that VFA should be used for vertebral fracture assessment.

The strengths of our study are that we included a broader range of children with chronic conditions and larger number of subjects compared to the previous paediatric studies. The increased image resolution of the contemporary bone densitometer enabled us to visualise and evaluate more vertebrae compared to older generation bone densitometers. This is the first study that differentiates agreement between techniques for the mild and clinically relevant moderate or severe osteoporotic fractures and has clearly demonstrated the superior agreement for the latter. In addition, we are the first to compare agreement between both techniques and raters.

The major limitation of this study was that we only used one experienced paediatric radiologist (R1) as the gold standard rather than consensus agreement between all raters. Since we used an adapted scoring system, identifying mild fractures as those with only 10% vertebral height loss, our results may not be directly comparable to others and it is possible that this may have resulted in a number of false positive fractures being reported.

To summarise, the use of VFA in children to identify moderate and severe vertebral fractures is as good as standard spinal radiography but has the significant advantage of substantially lower radiation dose to the child and is available at the point of care when a child has a routine bone density scan.

Conclusions

We conclude that the use of VFA using modern DXA scanners with superior visualisation is a practical and reliable method for the identification of clinically relevant vertebral fractures in children. Its ability to identify mild vertebral fractures is poor but comparable to conventional radiography. VFA by Lunar iDXA can be safely integrated into routine bone density assessment in children and adolescents and should largely replace the need for conventional radiography of the spine.

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Figure Legends

Figure 1 Examples of comparable radiographs and vertebral fracture assessment images. 1(a) & 1(b): Thoracic and lumbar radiographs and 1(c) VFA images of a 14-year-old boy with osteogenesis imperfecta with several mild and moderate vertebral fractures. 1(d) & 1(e): thoracic and lumbar radiographs and 1(f) VFA images of a 13-year-old girl with cystic fibrosis and no vertebral fractures.

Figure 2 Schematic representation of adapted Genant semi-quantitative vertebral fracture classification in selected vertebrae imaged by DXA (left) and radiograph (right)

Figure 3 Percentage of non-evaluable visible vertebrae combined for raters R1, R2 & R3 according to imaging modality and vertebral level. Black bars represent radiographs; grey bars represent VFA images. Non-evaluable vertebrae on radiographs = 219 (6.1%); and VFA images = 34 (0.9 %).

Figure 4 Percentage of vertebral fractures identified using the 'gold standard' (experienced radiologist using spine radiograph). Black bars represent severe vertebral fractures; grey bars represent moderate vertebral fractures and white bars represent mild vertebral fractures.

Table 1 Patient Descriptive Information (mean (SD)), n= 80 subjects.

	Mean (SD)	Range
Age (years)	12.0 (3.3)	5.1 – 18.8
Height (cm)	144.5 (19.6)	97 – 187
Height SDS	-0.6 (1.3)	-4.3 – 2.1
Weight (kg)	46.4 (19.3)	15.2 – 107.0
Weight SDS	0.4 (1.3)	-2.6 – 3.5
BMI (kg/m^2)	21.3 (5.3)	13.9 – 35.5
BMI SDS	0.9 (1.4)	-1.9 – 3.5
L2-L4 BMD (g/cm^2)	0.813 (0.18)	0.426 – 1.419
L2-L4 BMD Z-Score	-0.8 (1.2)	-3.9 – 2.6
L2-L4 BMAD (g/cm^3)	0.308 (0.05)	0.209 – 0.488
L2-L4 BMAD Z-Score	-0.4 (1.3)	-3.3 – 3.8

Table 2 Number (%) of vertebrae assessed per technique by Rater 1 (experienced paediatric radiologist)

	Radiograph	*VFA*	**MXA*
No fracture	933	999	625
	(77.8)	(83.2)	(52.1)
Mild fracture	121	128	344
	(10.1)	(10.6)	(28.6)
Moderate fracture	44	39	30
	(3.6)	(3.3)	(2.5)
Severe fracture	16	16	7
	(1.3)	(1.3)	(0.6)
Non-evaluable	79	9	185
	(6.6)	(0.8)	(15.4)
Not visible	7	9	9
	(0.6)	(0.8)	(0.8)
Total evaluable	1114	1175	1006
	(92.8)	(98.5)	(83.8)

* Due to the limitation within the GE Lunar iDXA Encore software™, MXA is only able to evaluate vertebrae from L4 to T4.

Table 3 Subjects (% of total) per vertebral fracture severity classified by Rater 1 (experienced paediatric radiologist)

Subjects with	*Radiograph*	*VFA*	*MXA*
No fracture	41 (51.3)	39 (48.7)	1 (1.3)
At least one mild fracture	26 (32.5)	28 (35.0)	66 (82.5)
At least one moderate fracture	8 (10.0)	7 (8.8)	8 (10.0)
At least one severe fracture	5 (6.2)	6 (7.5)	3 (3.8)
Total	80	80	**78

**GE Lunar Encore™ morphometric analysis failed on 2 out 80 subjects

Table 4 Kappa agreement (SE) between technique and rater (per vertebral level); on visible and evaluable scans.

Technique	*Rater*	*n*	*ANY Fracture*	*SEVERE Fracture*
RA	R1 vs. R2	1094	0.592 (0.031)	0.860 (0.036)
	R1 vs. R3	1092	0.534 (0.032)	0.810 (0.042)
	R2 vs. R3	1103	0.526 (0.033)	0.851 (0.039)
VFA	R1 vs. R2	1173	0.658 (0.030)	0.894 (0.039)
	R1 vs. R3	1168	0.600 (0.030)	0.836 (0.039)
	R2 vs. R3	1175	0.604 (0.030)	0.778 (0.049)
MXA	R4 vs. R5	987	0.361 (0.030)	0.793 (0.054)
	R4 vs. R5	977	0.384 (0.029)	0.776 (0.053)
	R5 vs. R6	982	0.406 (0.028)	0.691 (0.062)
RA vs. VFA	R1	1107	0.574 (0.032)	0.834 (0.038)
	R2	945	0.558 (0.031)	0.848 (0.042)
	R3	1102	0.527 (0.031)	0.826 (0.043)
VFA vs. MXA	R4	999	0.325 (0.028)	0.792 (0.052)
	R5	997	0.137 (0.022)	0.695 (0.065)
	R6	998	0.288 (0.024)	0.724 (0.055)

Table 5 Agreement with the gold standard between techniques for ANY fracture, per vertebral level and per subject and for SEVERE fracture per vertebral level and per subject

	ANY Fracture				*CLINICAL Fracture*			
	VFA Per vertebra	VFA Per subject	MXA Per vertebra	MXA Per subject	VFA Per vertebra	VFA Per subject	MXA Per vertebra	MXA Per subject
n	1111	80	952	78	1104	80	952	78
Kappa	**0.631**	**0.600**	0.323	0.419	**0.834**	**0.908**	**0.692**	**0.847**
95% CI	0.565-0.697	0.422-0.778	0.265-0.381	0.241-0.597	0.758-0.910	0.780-1.000	0.576-0.808	0.675-1.000
Sensitivity (%)	66.3	82.1	78.9	43.2	81.3	92.3	62.5	83.3
Specificity (%)	95.0	78.0	70.8	97.6	99.3	98.5	99.2	98.4
PPV (%)	71.5	78.0	33.9	94.1	87.3	92.3	81.1	90.9
NPV (%)	93.7	82.1	94.6	65.6	99.0	98.5	98.0	97.0
Agreement (%)	90.4	80.1	72.0	71.8	98.4	97.5	97.4	96.1
False +ve (%)	4.2	11.3	24.6	1.3	0.6	1.3	0.7	1.3
False –ve (%)	5.4	8.8	3.4	26.9	1.0	1.3	1.9	2.6

Gold standard is fracture identified by paediatric expert radiologist reading standard lateral radiograph; ANY represents ≥10% vertebral height reduction, CLINICAL (≥25% vertebral height reduction) ; VFA = vertebral fracture assessment; MXA = morphometric 6 point analysis; **Bold** highlights good (>0.6) to very good (>0.80) agreement between techniques.